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John J. Byrne, M.D.
John M. Cahill, M.D.
Edward A. Gaensler, M.D.
Denise Jouasset-Strieder, M.D.

Third (Boston University) Surgical Research Laboratory
Boston City Hospital, Boston, Massachusetts

PULMONARY VENTILATION AND DIFFUSION IN SHOCK

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ABSTRACT

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3. Investigators: John J. Byrne, M.D.
John M. Cahill, M.D.
Edward A. Gaensler, M.D.
Denise Jouasset-Strieder, M.D.

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The injection of gram negative endotoxin into the systemic venous system of dogs, generally causes a fall in lung compliance and a rise in resistance to airflow. These changes did not occur if the endotoxin was injected through the portal system. Heparin in average dosage was not effective in preventing the respiratory change.

The diffusing capacity of the canine lung for carbon monoxide (D_LCO) was generally diminished by systemic intravenous endotoxin and pulmonary capillary blood volume (Vc) fell significantly.

In humans, D_LCO increases with increasing lung volume (V_L) due primarily to a rise in Vc. The ratio Vc/V_L does not change with increasing V_L in normal subjects, and may provide a useful standard for the study of patients.

KEY WORDS:
SHOCK - PULMONARY VENTILATION - PULMONARY DIFFUSION - COMPLIANCE AIRWAY RESISTANCE - ENDOTOXIC SHOCK - PULMONARY CAPILLARY BLOOD VOLUME - LUNG VOLUME -

A. COMPLIANCE AND AIRWAY RESISTANCE

1. Studies in dogs.

We have reported previously on changes in the ventilatory mechanics during hypovolemic and endotoxic shock.[1-2-3-4] We noted a rise in compliance and a fall in resistance to airflow during acute hypovolemic shock. Following the intravenous injection of endotoxin we noted in general a tendency for compliance to fall and resistance to airflow to rise. Heparinization of the animal prior to the injection of endotoxin appeared to interfere with this response. During the past year we have attempted to evaluate more carefully this response to endotoxin especially with relation to varied dosage and heparinization. The ability of the liver to neutralize endotoxin has also been investigated. We have studied, in addition, the early effect of intraperitoneal sepsis caused by contamination with liquid feces.

Methods

The method utilized in determining the airflow resistance and lung compliance of dogs has been discussed previously and described in detail.[1-3] A series of 21 dogs were studied and divided into four groups.

In Group I following control studies six dogs were given gram negative endotoxin intravenously in varied dosage and ventilatory mechanics studied thereafter.

Group II consisted of six dogs fully heparinized and then treated in a manner similar to the dogs in Group I. Two of these dogs were given 1 ml. of endotoxin per kilo. of body weight and four of them received 2 ml. of endotoxin per kilo.

Group III consisted of four dogs in which following anesthesia the abdomen was opened, the splenic vein isolated and cannulated with a polyethylene catheter. The abdomen was then closed tightly around the catheter and the animal placed in the body plethysmograph. Following control studies endotoxin was administered intravenously through the splenic vein. One dog was given a dose of 2 ml. per kilo and the other three received 4 ml. per kilo of body weight.

Five dogs in Group IV had control studies carried out; the dogs were then removed from the plethysmograph and strained fecal material diluted in 150 cc. of saline was injected into the peritoneal cavity. The animals' ventilatory mechanics were then studied for three to five hours following the procedure.

Results

In Table I are grouped eleven dogs given endotoxin through the systemic vein. None of these animals received heparin. Five dogs (I-V) were reported previously[2] with the results corrected in one case (V). The other six animals comprise Group I studied during this year. The dosage of endotoxin varied as indicated. Blood pressure fell in ten of eleven dogs but a marked fall was noted in only seven. Lung compliance fell in eight, was unchanged in two and rose in one animal. Resistance rose in seven animals, fell in three and was essentially unchanged in one.

The results in the second group of dogs is listed in Table II. These six dogs were fully heparinized prior to administration of gram negative endotoxin. In all six of these animals both the compliance and blood pressure fell significantly. Resistance rose in four, fell in one and was unchanged in one.

Table III indicates the results in four non-heparinized dogs given endotoxin through the splenic vein. In this instance the blood pressure fell in each case. Resistance to airflow also fell in all four of the animals but a fall in compliance was noted in only one.

The five dogs in Group IV were subjected to peritonitis due to the instillation of liquid feces. The results are listed in Table IV. No definite trend was noted in this group. Resistance rose markedly in one dog (II). This animal was sick to begin with and had a marked purulent discharge from the nose. The initial resistance was high at 9 cm. $H_2O/L/$ sec., rose fourfold rapidly and the animal died in four hours. Dog five (V) had a gradual increase in resistance accompanied by a rising compliance. Dog three (III) tended toward an increased resistance with a fall in compliance. The other two animals were essentially unchanged during the period of study. All died within twelve hours.

Discussion

The administration of endotoxin into the systemic vein generally resulted in a rise in resistance to airflow and a fall in lung compliance, as others[5] have noted. In this series, no good relationship could be noted between the size of the dose and the magnitude of the response. Heparin 10,000 USP units given I.V. prior to endotoxin administration failed to prevent the response, contrary to our first impressions.[2] A protective action by Heparin has been noted by others.[5] Two major problems in this study deserve mention. The first is the possibility that the resistance of the animal to endotoxin varies. The second is the known variation in the potency of the endotoxin. We were able to check this only grossly and at

intervals. One mixture used in a number of dogs proved to have little potency and the studies were discarded. The ineffectiveness of Heparin was a surprise. Our own initial results with Heparin[2] were noted by accident and at a time when we were unable to check on the potency of the endotoxin so we decided to continue the study with more potent material. We do not conclude that Heparin is of no value at all but certainly not in the dosage used (10,000 units per dog) in conjunction with the amount of endotoxin we gave.

When the endotoxin was administered through the portal system the lung changes were largely prevented, although the blood pressure did fall. Since the dose of endotoxin was rather large, it indicates that the liver has a large capacity for inactivating this material. Either the circulatory response is more sensitive than the lung response or the factor causing it is not removed by the liver. It will be of interest to see if even larger doses of endotoxin, similarly administered can overcome this protective effect.

The effect of peritonitis requires considerably more study especially just prior to the death of the animal. Only two studies were carried out near death (II-V). We are attempting to investigate this period at present and also to increase the survival time to see if the lung changes become significantly worse as has been predicted.[6-7] The marked change in dog two (II) is interesting in view of the known respiratory disease. Any similarly ill dogs will also be studied and lung specimens obtained at death.

2. Studies on humans

Nine additional studies of Ward patients have been carried out. Seven were preoperative problems; two were studied while on Aramine with a normal blood pressure and then during the attempted withdrawal of the drug with a

moderate hypotension. Both of these patients, several days prior to the study had a probable pulmonary embolus. Both were postoperative and both recovered. Patient R.A. had a marked hypoxemia even on high concentrations of oxygen. Unfortunately, the equipment for measuring lung volume had not arrived at the time of these studies. The results are listed in Table V.

SYSTEMIC ENDOTOXIN - NO HEPARIN

TABLE I

DOG	WEIGHT	DOSE	Mgm/Kg.	CONTROL B.P.	C	R	IMM. POST-ENDOTOXIN B.P.	C	R	½ - 2 Hrs. B.P.	C	R
I	10	20	2.0	120/77	.05	3.0	44/14	.02	9.0	88/55	.04	3.3
II	13	20	1.5	140/110	.07	2.2	60/40	.05	3.0	50/56	.08	2.7
III	10	20	2.0	91/54	.09	3.0	70/38	.09	2.3	50/27	.10	2.7
IV	14	20	1.5	145/124	.07	1.8	low	.04	2.1	82/55	.03	1.6
V	10	20	2.0	135/100	.04	3.4	135/108	.04	3.5	108/84	.05	4.0
VI	13	6	0.5	171/120	.07	3.1	95/67	.09	2.5	151/100	.07	2.6
VII	17	13	0.75	170/110	.09	3.3	93/66	.05	4.0	116/93	.09	3.1
VIII	17	20	1.2	200/140	.08	4.0	170/85	.07	4.3	195/134	.03	4.1
IX	11	10	1.0	154/112	.05	3.8	63/28	.02	11.0	100/74	.04	3.8
X	14	9	0.6	151/112	.04	5.5	145/112	.03	6.2	99/73	.04	5.0
XI	10	30	3.0	140/86	.08	4	86/68	.05	3.1	91/68	.03	4.1

Weight = Kilograms
Dose = Mgm. of Endotoxin
B.P. = Blood Pressure in mm. Hg.
C = Lung Compliance in liters/cm.H_2O
R = Resistance to airflow in cm.H_2O/liter/sec.

TABLE II

SYSTEMIC ENDOTOXIN - HEPARINIZED

DOG	WEIGHT	DOSE	Mgm/Kg.	CONTROL B.P.	C	R	IMM. POST-ENDOTOXIN B.P.	C	R	½ - 1 Hr. B.P.	C	R
I	10	10	1.0	145/105	.06	3.2	66/50	.04	3.2	81/63	.06	2.7
II	13	26	2.0	144/100	.06	5.6	65/49	.03	4.6	108/72	.06	4.9
III	11	22	2.0	126/93	.04	4.6	37/30	.01	6.9	74/59	.04	3.8
IV	17	34	2.0	137/104	.07	4.6	low	.02	6.1	81/59	.1	3.0
V	10	20	2.0	112/91	.15	3.0	88/70	.03	3.6	71/50	.03	2.9
VI	10	10	1.0	150/120	.04	4.0		.02	4.3	94/75	.05	2.2

Wt.Kg. = Kilograms
Dose = Amt. of Endotoxin
B.P. = Blood Pressure in mm. Hg.
C = Lung Compliance in liters/cm. H_2O
R = Resistance to airflow in cm. H_2O/liter/sec.

TABLE III

SPLENIC VEIN SERIES

DOG	WEIGHT	DOSE	CONTROL B.P.	CONTROL R	CONTROL C	IMM. POST-ENDOTOXIN B.P.	IMM. POST-ENDOTOXIN R	IMM. POST-ENDOTOXIN C	½ - 1 Hr. B.P.	½ - 1 Hr. R	½ - 1 Hr. C
I	13	26	135/107	6.8	.11	60/50	4.1	.12	113/74	5.0	.10
II	16	64	151/103	2.9	.10	51/43	2.4	.07	117/94	2.8	.10
III	14	56	168/134	4.2	.05	114/87	3.0	.05	134/107	3.4	.05
IV	10	40	126/100	3.8	.09	44/35	1.6	.14	139/107	2.0	.12

Weight = Kilograms
Dose = Mgm. of Endotoxin
B.P. = Blood Pressure in mm. Hg.
C = Lung Compliance in liters/cm.H_2O
R = Resistance to airflow in cm.H_2O/liter/sec.

TABLE IV

		CONTROL			1 HOUR FOLL. PERITONITIS			1 HOUR			2 HOURS			4 HOURS		
DOG	Wt.	BP	R	C	BP	R	C	BP	R	C	BP	R	C	BP	R	C
I	11	150/110	2.4	.07				140/105	2.3	.08	125/100	2.2	.05	150/120	2.3	.06
II	12	130/80	9.0	.05	130/80	37.0	.04	145/100	37.0	.03	135/100	32.0	.02		DEAD	
III	21	135/90	2.1	.11	135/105	3.4	.08				110/85	3.4	.09	110/80	4.3	.09
IV	11	125/95	4.2	.09	130/100	3.1	.10				125/100	4.1	.09	110/95	3.4	.11
V	14	155/105	2.5	.08	160/120	2.6	.07	180/130	2.4	.09	150/100	2.6	.09	50/30 → 155/95	4.1	.19
												3 HOURS				
											140/95	7.2	.13			

TABLE V

Pt.	SEX	AGE	TOBACCO	LUNG DISEASE	R	C	POSITION
M.M.	M	68	Heavy in past	SOB - 2 blocks	8.6 6.5	.11 .14*	Sitting
I.F.	F	67	0	None - Very Obese W.T.-205 - Ht. 5'3"	5.5	.06	Sitting
H.K.	F	58	1-2 pks./day	Asthma - Frequ. Prevs. Takes pills for Asthma.	13.3	.14	Sitting
W.S.	M	60	½-1½ pks./day	Cough DOE - scarring by x rays. AP inc. BS dis.	2.9	.31	Sitting
E.O.	M	68	3-4 cigs./day	Hx. Diabetic-Ht. disease Past Congest. Failure	2.7	.16	Sitting
G.R.	M	53	1-1½ pks./day	Wheezes-"Emphysema" DOE - Chr. Alc.	6.8	.11	Sitting
A.B.	M	84	0	Prev. Congest. Failure Occ. DOE&PND - lungs clear	1.5	.23	Sitting

* After Isuprel

SHOCK PATIENTS

Pt.	SEX	AGE	LUNG DISEASE	BLOOD PRESSURE	R	C	POSITION
J.M.	M	83	Pulmonary Embolus	on Aramine - 120/70	3.2	.12	Semi Sitting
				off Aramine - 95/70	1.5	.16	Semi Sitting
R.A.	M	70	Pulmonary Embolus	on Aramine - 160/100	11.0	.08	Left Side
				off Aramine - 80/?	11.0	.06	Left Side

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B. PULMONARY DIFFUSION STUDIES

1. Studies in dogs.

The diffusion capacity for carbon monoxide (D_LCO) was studied in dogs using the single-breath technique. The results of the studies in anemia, acute hypotension, irreversible hemorrhagic shock, after early retansfusion and the effect of prolonged anesthesia have been reported[1] and are summarized in Figure I.

The present studies were carried out to investigate the effect of the intravenous injection of gram negative endotoxin on the D_LCO and pulmonary capillary blood volume (Vc). They comprise our first effort to utilize our new equipment for the diffusion studies.

Method

The technique for studying D_LCO, Vc and Dm (membrane diffusion) in dogs has been described previously.[1-2-3-4] In the present studies however, alveolar PO_2 was measured by a Beckman E-2 Oxygen Analyzer and alveolar PCO_2 by an Instrumentation Laboratory CO_2 electrode. These had been measured previously by the Scholander technique.

A total of five dogs were anesthetized lightly with Pentathol and control studies carried out. Each animal was then given intravenous endotoxin and shortly thereafter the studies were repeated. The hematocrit was obtained on all animals before endotoxin but on only three post-endotoxin. Pulmonary capillary red cell mass (Vrbc) was obtained from the Vc and the hematocrit. The ratio $D_L/Vrbc$ = Drbc was also calculated, both for the present studies and for those reported previously.[1] Drbc equals the diffusing capacity of 1 ml. of red blood cells in the lung capillaries.

Results

Table I indicates the results obtained in the five dogs. In dogs I and II the results in shock are calculated on the basis of there being no change in the original hematocrit and are therefore probably incorrect but demonstrate the same trend seen in the other three studies.

In each instance a marked fall in Vc occurred and in general a fall in D_L. Dm was even more variable than in the past and reached infinity on three of these studies.

Dog V was studied immediately after endotoxin and then about 15 - 30 minutes later. Vc rose briefly in this animal and then fell abruptly in the second study.

Discussion

The effect of intravenous injection of gram negative endotoxin on pulmonary diffusion and capillary blood volume appears to be a fall in Vc and in general a fall in D_LCO. This is essentially similar to the effect of acute shock as noted in Figure I. At the time that these studies were done the blood pressure was in each instance well below the normal level. The result in Dog V in which the Vc initially rose is of interest, since according to other authors endotoxin causes a release of Serotonin[5] in the lung and it is known that Serotonin is a pulmonary vein constrictor and causes an increase in pulmonary capillary blood volume.[6] A later effect of endotoxin is believed to be the development of intracapillary clotting.[7] The possibility exists that the Serotonin effect on the pulmonary venous circulation is of relatively short duration and is superceded immediately by the effect of intracapillary clotting and a fall in Vc due to a diminished capillary bed in the lung.

These preliminary studies indicate that if endotoxin causes a Serotonin-like effect on the lung, it is of short duration and diffusion studies must be done immediately after the endotoxin is administered to demonstrate it. Furthermore, there is a rapid rise in hematocrit after endotoxin and it will have to be measured frequently in order to get accurate diffusion results. The hematocrit of Dog V rose from a control of 48 to a high of 64 toward the end of the study. Both of the post-endotoxic results were based on a hematocrit of 64 but at the time of the first study it was probably a good deal lower. The late effect of endotoxin on the lung after the blood pressure has returned to normal is also planned for study.

Figure II shows the relationship of D_L to Vrbc in 24 control studies, in six studies of acute hypovolemic shock and in six of irreversible shock reported previously.[1] The line of maximal D_{L120} has a slope of 1.4 which is the "diffusing capacity" of 1 ml. of RBC directly exposed to alveolar air. The experimental data show that the RBC in pulmonary capillaries have a somewhat lower "diffusing capacity". $D_L/Vrbc = Drbc$, averages .85 $\pm$ 16 ml./min./mm. Hg./ml. RBC for the experiments in Figure II. The shaded area in Figure II would then correspond to increased membrane thickness.

2. Studies in humans.

The effect of varying lung volume (V_L) on the pulmonary-capillary blood volume (Vc) and the membrane-diffusing capacity (Dm) was studied in twelve normal volunteers. The purpose of this study was to set a standard for evaluating results in acutely ill patients who might be unable to hold their breath at total lung capacity.

Method

Twelve normal volunteers were studied, ages 18 to 51. Their biometric data was obtained and is shown in Table II. Vital capacity and timed-vital capacity were measured with a Gaensler vitalometer and the residual volume by the closed-circuit helium dilution method. Total blood volume and hematocrit were determined in seven subjects by the radioactive albumin technique. The diffusion capacity (D_L) was measured by the single-breath method using carbon monoxide, as modified by Foster et al.[9] The subject was asked to perform a complete expiration, followed by inspiration of the test gas and ten seconds of breath-holding. This was followed by a rapid expiration from which an alveolar sample was collected. In each subject the lung volume at which the breath was held was approximately at total lung capacity and at approximately two-thirds of total lung capacity. Two subjects were also studied at one-third of total lung capacity. Three gas mixtures were used as in previous studies, all containing .3 per cent carbon monoxide, 10 per cent helium but with 20, 50 or 90 per cent oxygen. The balance was nitrogen. A box-balloon spirometer permitted the recording of inspired volume, breath-holding time and dead-space washout volume. The alveolar gas samples were analyzed as in previous studies and D_L, Vc and Dm calculated by methods described previously.[2] Duplicate measurements of D_L were made with each gas mixture and at each lung volume. The volume of red cells in the lung capillaries (Vrbc) was estimated from the pulmonary-capillary blood volume and the hematocrit, and the ratio of diffusion capacity to the volume of red blood cells (Drbc) was calculated.

Results

In Table III are listed the values of D_L, Vc and Dm at the varying lung volumes. In general D_L and Vc decreased markedly with decreasing lung volume while Dm was not altered significantly.

Figure III demonstrates the percentage relationship of Vc to lung volume for each individual, comparing himself to his best performance. It is noted that Vc fell proportionately as lung volume decreased. The fall in D_L with decreasing lung volume was relatively less than that of Vc. However, when D_L and Vc were compared to the lung volumes in absolute values, a proportional relationship was shown in both instances, as demonstrated by Figures IV and V. The results of a similar analysis for Dm indicated the absence of any meaningful trend.

Table IV is another representation of the relationship between the diffusion data and the lung volume. It indicates that the amount of capillary blood per liter of lung volume remains constant as the lung volume changes, averaging 13.5 ml. per liter of lung volume, but both D_L and Dm per liter of lung volume decreased with increasing lung volume.

Discussion

This study confirms the large changes in D_L that are induced by changing lung volume[10] and it demonstrates that a proportional increase in capillary-blood volume is the dominant mechanism of the D_L changes. The volume dependence of D_L is of practical importance for the definition of normal values and the appreciation of pathological changes when using the standard single-breath technique. Differences in the proposed

prediction formula may result, not only from the relatively small number of subjects usually studied and the possible difference in analytic techniques but also from unequal efforts to reach total lung capacity. Vc increases proportionately with increasing lung expansion and this implies that the capillary bed expands at the same rate as the alveoli augment in size and number. Opposite changes have been observed in isolated lung preparations[11] and no sure explanation can be offered at present for this difference. The lung volume dependence of Vc limits the significance of its relationship to total blood volume as seen in Table IV unless V_L (lung volume) is known. The amount of capillary blood per liter of lung volume appears to offer a better index of the total perfusion of the lungs. Our predicition formula, Vc equals 13.5 ml. per liter of lung volume applies generally to any lung volume.

The absence of any change in average Dm when the lungs are distended from 65 to 95 per cent was somewhat surprising. It implies that the alveolar membrane is left unaltered or that any increase in its surface area is cancelled by an increase in its thickness. We favor the latter mechanism on the basis of our previous observations,[2] which support the hypothesis that the alveolar membrane is useful for gas exchange only where it is in contact with red blood cells. In this hypothesis a rise in Vrbc is synomous with an increase in effective surface area and a fall in Drbc with an increased thickness of the membrane. Both changes are observed with progressive distension of the lungs and the composition of the two effects accounts for pattern of changes in D_L. A cause for the behavior of Vc and Dm with

increasing lung volume could be found in a concomitant increase in the surface tension of the alveolar lining which would induce the opening of capillaries and exudation of fluid within the membrane.[12] The rapid degradation of this surfactant material when exposed to air in vitro may then offer an explanation f or the different behavior of Vc in isolated lungs.

We believe that the amount of capillary blood per liter of lung volume may prove to be an important parameter for study since it does not change under normal conditions with variations in lung volume. It establishes a solid basis for comparison with studies carried out during shock or other pathologic states.

TABLE I

DOG	DIFFUSION IN ENDOTOXIC SHOCK CONTROL D_{L120}	Vc	Dm	Vrbc	D_L/Vrbc	AFTER ENDOTOXIN D_{L120}	Vc	Dm	Vrbc	D_L/Vrbc
I	18.8	57	29	28	.67	11.6	20	46	10	1.16
II	17	33	34.5	16.5	1.03	19	16	Inf.	8	2.3
III	33	85	61	40	.81	22	31	Inf.	17	1.3
IV	24	72	51	28	.85	17	32	103	14	1.2
V	18.7	34	98	16	1.17	* 16	52	18	33	.48
						** 14	17	Inf.	11	1.3

Underlined results are based on assuming the hematocrit remained unchanged in endotoxic shock. The changes, however, are similar to those seen in the other animals.

D_{L120} = $\frac{\text{ml./min.}}{\text{mm. Hg.}}$

Vc = ml.

Dm = $\frac{\text{ml./min.}}{\text{mm. Hg.}}$

Vrbc = $\frac{\text{ml./min.}}{\text{mm. Hg.}}$

Inf. = Infinity

* = Immediately following Endotoxin

** = 15 - 30 minutes after Endotoxin

TABLE II

Biometric data for 12 normal male volunteers. Age in years, height in meters, weight in Kg; vital capacity (VC) and total lung capacity (TLC) in liters BTPS; one-second timed vital capacity (TVC) and residual volume to total lung capacity ratio in per cent. Total blood volume (TBV) in liters and hematocrit (Hct) in per cent.

	Age	Height	Weight	VC TVC	TLC RV/TLC	TBV Hct
G.M.	18	1.78	69	4.61 86	5.74 20	4.81 49
E.G.	23	1.92	96	6.75 78	8.43 20	6.09 49
J.R.	28	1.73	75	6.18 80	7.68 20	4.72 46
G.P.	31	1.88	74	6.92 70	8.97 23	5.29 46
S.I.	31	1.65	69	4.59 70	5.73 23	5.29 46
R.K.	32	1.78	71	5.10 87	6.04 15	—
G.C.	34	1.78	105	4.50 80	6.87 34	—
W.G.	34	1.90	93	6.85 67	8.30 21	—
A.T.	35	1.77	74	5.06 84	6.78 25	5.30 45
J.C.	39	1.83	91	5.05 72	6.90 27	5.19 48
R.C.	44	1.84	105	5.02 83	7.13 27	—
W.H.	51	1.82	67	3.38 70	6.08 44	—

TABLE III

Diffusion data for 12 normal male volunteers. The lung volumes (V_L) are indicated in per cent of total lung capacity (TLC). D_L is the diffusing capacity of the lungs in ml/min/mm Hg, Vc the pulmonary capillary blood volume in ml and Dm the diffusing capacity of the alveolar membrane in ml/min/mm Hg.

	1/3 TLC				2/3 TLC				TLC			
	V_L	D_L	Vc	Dm	V_L	D_L	Vc	Dm	V_L	D_L	Vc	Dm
G.M.					63	34	92	60	95	44	109	105
E.G.					59	24	52	70	99	47	[illegible]	200
J.R.					70	30	78	65	92	34	109	60
C.P.					57	35	76	100	96	47	137	90
S.I.					64	22	50	70	95	27	74	60
R.K.	36	19	29	80	74	24	55	50	90	31	66	75
G.G.					54	30	49	210	97	46	120	100
W.G.	34	19	37	50	60	27	50	150	94	40	93	200
A.T.					66	30	82	60	94	41	110	85
J.C.					67	24	45	100	95	28	106	45
R.C.					79	37	63	250	96	41	74	200
W.H.					67	18	34	70	98	26	51	90
Mean ± SD	35	19	33	65	65 ± 7	28 ± 7	60 ±18	103 ± 58	95 ± 2	38 ± 9	94 ±25	109 ± 66

TABLE IV

Diffusion data per liter of lung volume (V_L) at three different fractions of total lung capacity (TLC) D_L, Vc and Dm as in Table II. The ratio of pulmonary capillary blood volume to total blood volume (Vc/TBV) is also indicated. The figures are mean values ± standard deviation.

	1/3 TLC	2/3 TLC	TLC
DL/V_L	7.8	6.2 ± 1.4	5.6 ± 1.3
Vc/V_L	13	13 ± 4	14 ± 3
Dm/V_L	28	23 ±12	16 ± 7
Vc/TBV		1.3 ± 0.3	.0 ± 0.4

Figure I

CHANGE IN DL,Vc AND Vrbc IN ANEMIA AND SHOCK

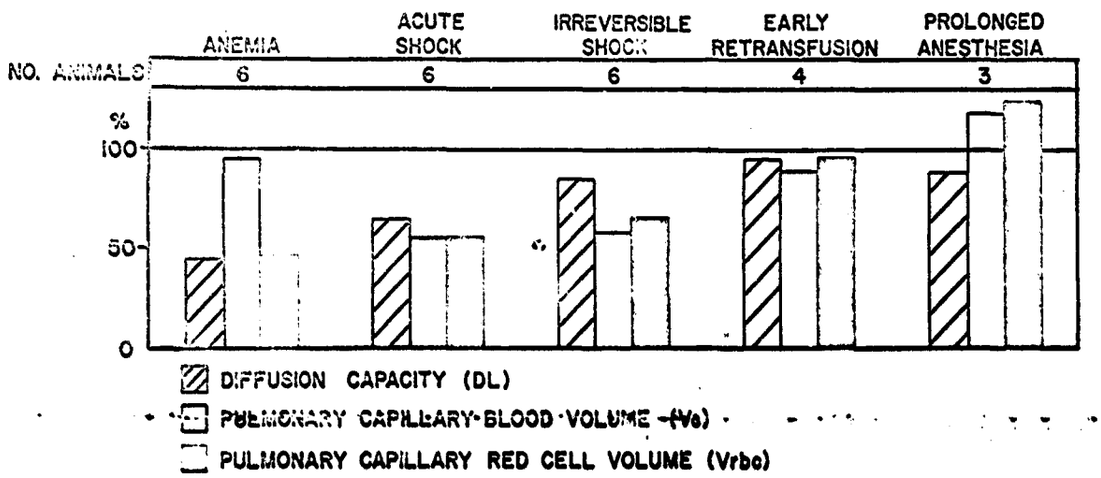
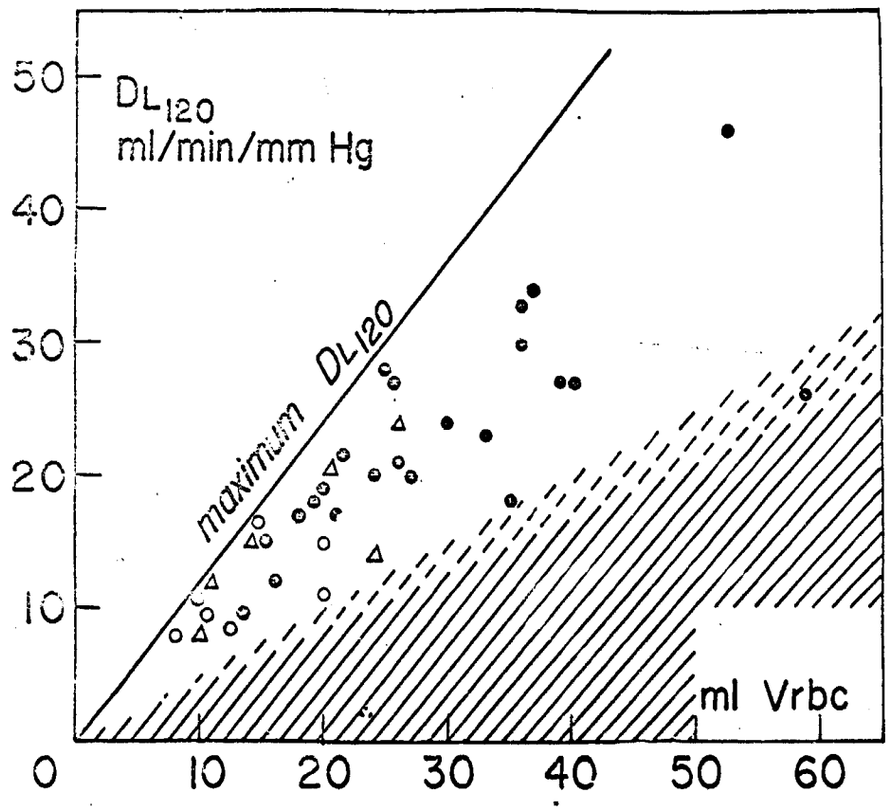


Figure II



Relationship between diffusing capacity, at a capillary oxygen tension of 120 mm. Hg. (D_{L120}) and volume of red blood cells in the lung capillaries (Vrbc). The line of maximal D_{L120} has a slope of 1.4 which is the "diffusing capacity" for CO of 1 ml. of red blood cells when blood is directly exposed to alveolar air containing CO, i.e. when the membrane diffusing capacity tends toward infinity. Any "thickening" of the alveolar capillary membrane should cause the points on this diagram to fall in the shaded area. ○ Controls, ○ Acute Hypovolemic Shock, △ Irreversible Shock

Figure III

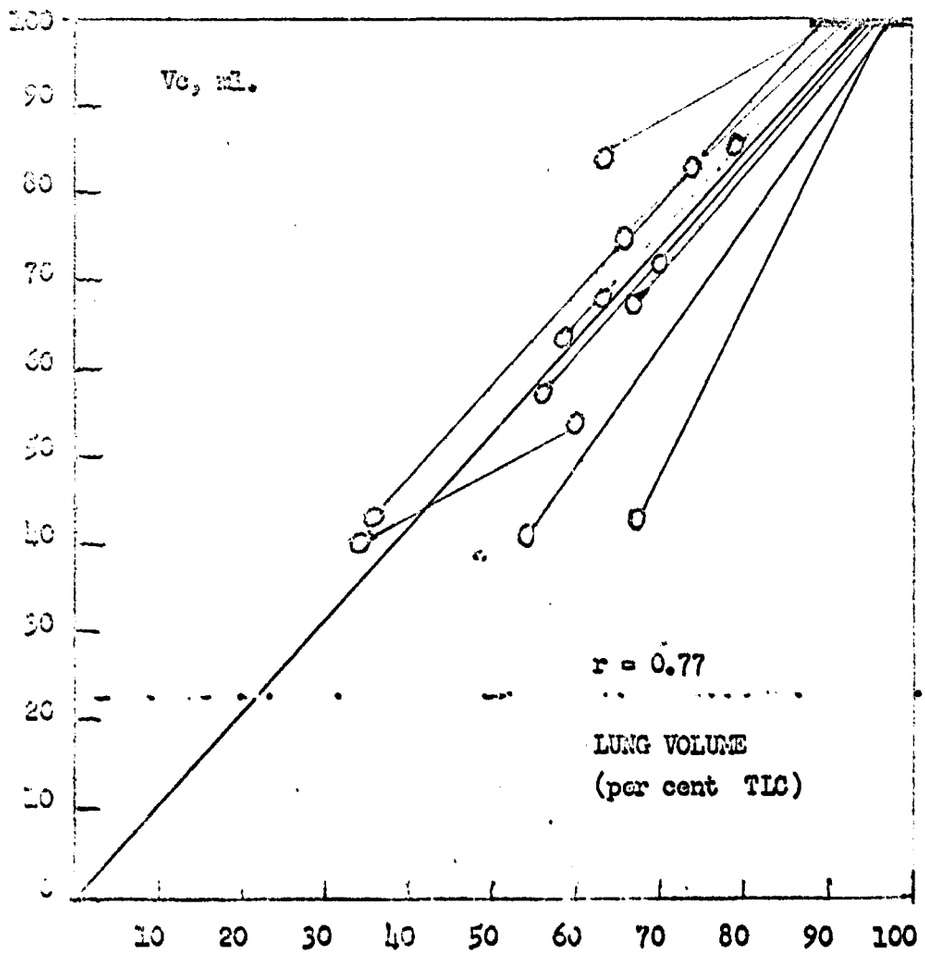

Vc, ml.
100
90
80
70
60
50
40
30
20
10
0
r = 0.77
LUNG VOLUME
(per cent TLC)
10
20
30
40
50
60
70
80
90
100

Figure IV

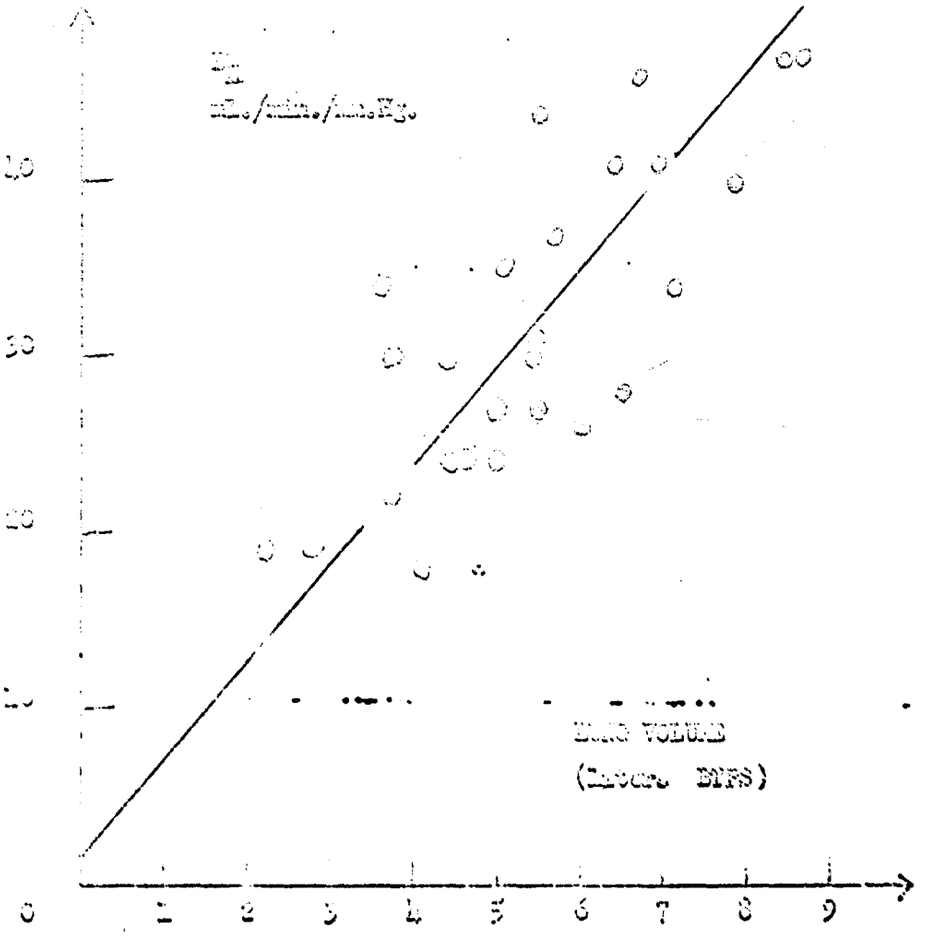
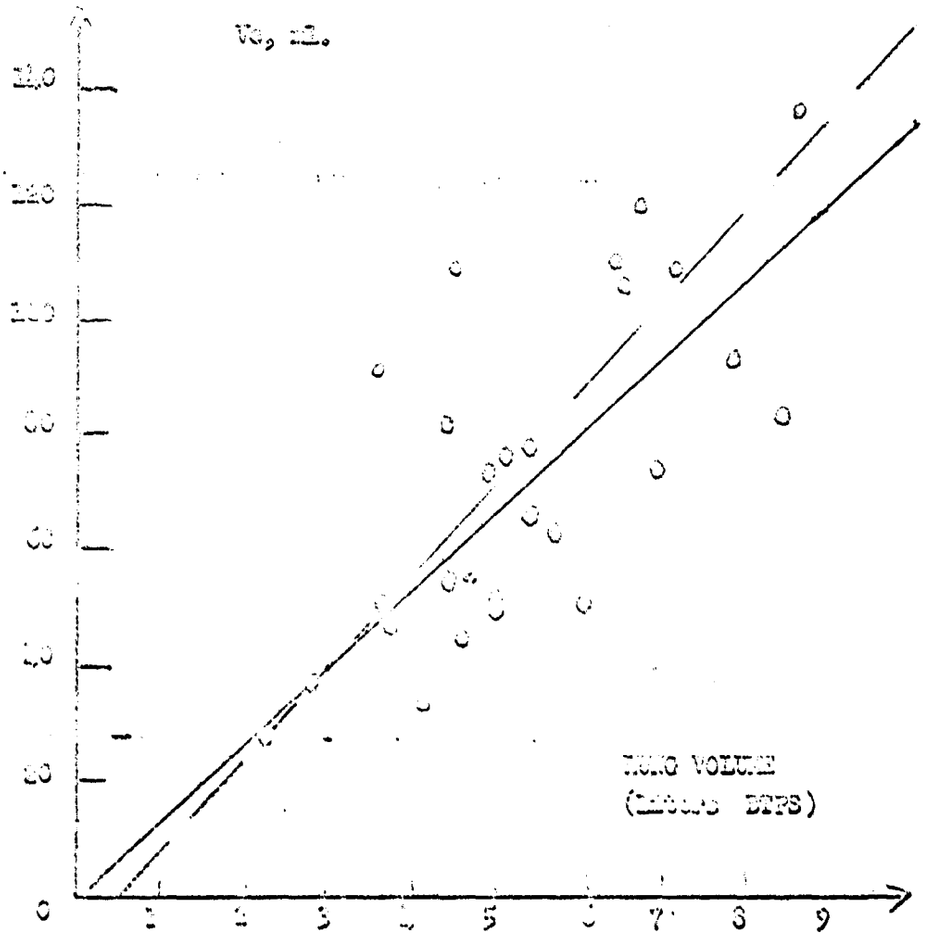


Figure V



Solid line - Ve = 15.5 ml. per liter of tidal volume

D. line - Experimental regression line
Ve = 1.5 V_T minus 7.35

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